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Convenient construction of diverse chromene frameworks via three-component reactions

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Full Research Paper

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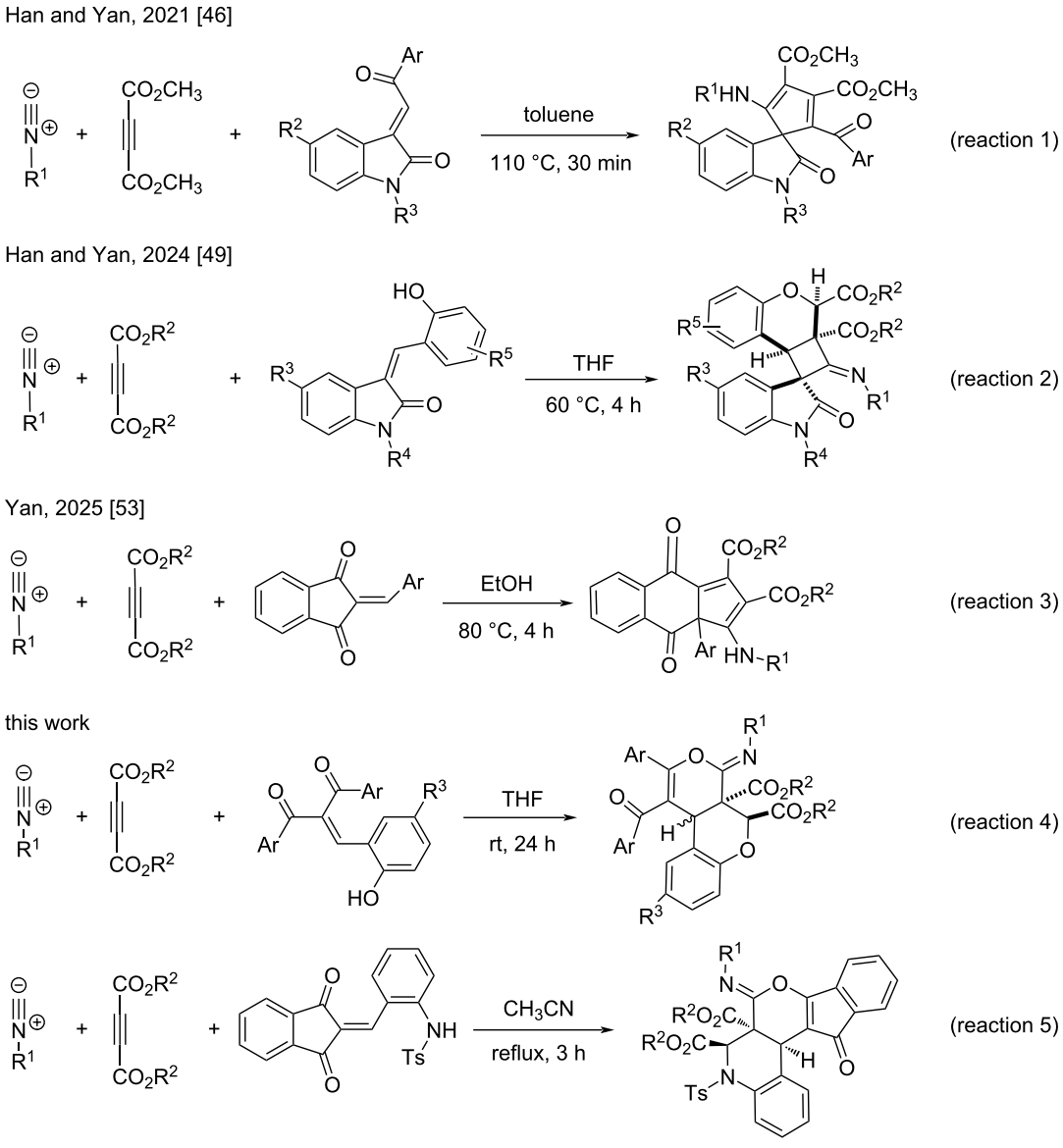
Abstract

The three-component reaction of alkyl isocyanides, dialkyl but-2-ynedioates and 2-(2-hydroxybenzylidene)-1,3-diarylpropane-1,3-diones afforded diastereomeric pyrano[3,4-*c*]chromenes with major diastereomers in 26–52% yields and minor diastereomers in less than 24% yields. On the other hand, the three-component reaction of alkyl isocyanides, dialkyl but-2-ynedioates and with 2-(2-*N*-tosylaminobenzylidene)-1,3-indanediones gave tetrahydroindeno[2',1':5,6]pyrano[3,4-*c*]quinolines in moderate to good yields. In addition, the domino reaction of arylamines, dialkyl but-2-ynedioates and 2-(2-hydroxybenzylidene)-1,3-diarylpropane-1,3-diones afforded functionalized chromenes in satisfactory yields. Therefore, a convenient synthetic method for diverse functionalized chromenes was successfully developed by three-component reaction of alkyl isocyanides, dialkyl but-2-ynedioates and various α,β-unsaturated diketones.

Introduction

Alkyl isocyanides are very special functionalized compounds with high reactivity to both electrophilic and nucleophilic reagents [1,2]. Therefore, alkyl isocyanides are one of the most important and frequently used synthons for the efficient synthesis of various N-containing acyclic and heterocyclic compounds [3,4]. Furthermore, alkyl isocyanides have high compatibility with versatile electrophilic and nucleophilic reagents, which enabled them to be key substrates in multicomponent and domino reactions [5-12]. In the past years, many isocyanide-based multicomponent reactions have been successfully developed [13-23]. It was well-known that the Passerini reaction, Ugi reaction, Orru reaction and van Leusen reaction with alkyl isocyanides as key substrates have become famous multicomponent reactions [24-28] and have become the most powerful tools for rapid construction of various nitrogen-containing compounds [29-31]. In recent years, the multicomponent reactions

based on employing both alkyl isocyanides and electron-deficient alkynes as key substrates have attracted widespread interests [32-35]. In these multicomponent reactions, the initially nucleophilic addition of alkyl or aryl isocyanides to electron-deficient alkynes generated in situ a 1,4-dipolar intermediate, which in turn was trapped by various reagents to give diverse acyclic or cyclic compounds [36-45]. In recent years, we have concentrated on the developing multicomponent reactions based on employing isocyanides and electron-deficient alkynes as key substrates. Several multicomponent reactions were successfully provided for efficient synthetic protocols for diverse polycyclic O,N-containing heterocyclic compounds [46-54]. For example, a three-component reaction of alkyl isocyanides, dialkyl but-2-ynedioates and 3-methyleneindolin-2-ones in refluxing toluene allowed the convenient formation of spiro[cyclopentane-1,3'-indolines] in satisfactory yields (Scheme 1, reaction 1) [46]. When 3-(*o*-hydroxyarylidene)indolin-2-ones were used in the above three-component reactions, polycyclic spiro[cyclobuta[*c*]chromene-1,3'-indolines] were obtained in good isolated yields with high diastereoselectivities (Scheme 1, reaction 2) [49]. When 3-(*o*-hydroxyphenacylidene)indolin-2-ones were employed in the reaction, spiro[benzofuran-3,2'-furans] were produced in good yields with high diastereoselectivities [52]. In addition, the three-component reaction of alkyl isocyanides, dialkyl but-2-ynedioates and 2-arylidene-1,3-indanediones in ethanol under refluxing conditions allows the



Scheme 1: Representative multicomponent reactions based on isocyanides and but-2-ynedioates.

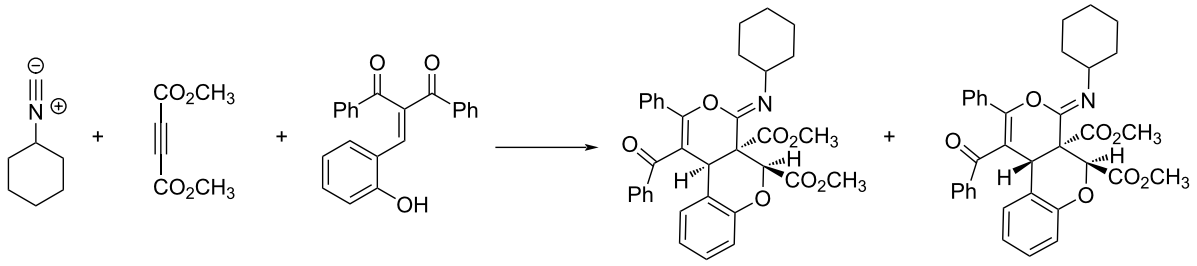
formation of functionalized cyclopenta[*b*]naphthalenes (Scheme 1, reaction 3) [53].

In continuation of our program on the development of convenient multicomponent reactions with isocyanides and electron-deficient alkynes for the construction of diverse heterocyclic compounds [54-60], herein, we wish to report three-component reactions of alkyl isocyanides, dialkyl but-2-ynedioates and 2-(2-hydroxybenzylidene)-1,3-diarylpropane-1,3-diones or 2-(2-*N*-tosylaminobenzylidene)-1,3-indanediones for the convenient syntheses of functionalized pyrano[3,4-*c*]chromenes (Scheme 1, reaction 4) and tetrahydroindeno[2',1':5,6]pyrano[3,4-*c*]quinolines (Scheme 1, reaction 5).

Results and Discussion

Initially, the reaction conditions were examined by using cyclohexyl isocyanide (**1a**), dimethyl but-2-ynedioate (**2a**) and 2-(2-hydroxybenzylidene)-1,3-diphenylpropane-1,3-dione (**3a**) as standard on the basis of our previously reported reactions [46-53]. The main results are summarized in Table 1. The three-component reaction in different solvents such as dichloromethane (DCM), acetonitrile (MeCN) and dichloroethane (DCE) at room temperature for 24 hours resulted in a mixture of the diastereomeric products **4a** and **4a'** in very low yields (Table 1, entries 1–3). However, the reaction in tetrahydrofuran (THF) at room temperature for 24 hours gave the product **4a** in 52% yield as major product and the product **4a'** in 12% yield as minor product (Table 1, entry 4). On the other hand, no reaction was observed in methanol (Table 1, entry 5). The structural analysis indicated that two products **4a** and **4a'** are belonging to two diastereomers. Then, the reaction in different solvents at elevated temperatures also afforded the two products **4a** and **4a'** in low yields (Table 1, entries 6–11). On the other hand, the three-component reaction was completely inhibited when some organic bases such as DABCO (1,4-diazabi-

Table 1: Optimizing reaction conditions.[a]



1a **2a** **3a** **4a** **4a'**

entry	ratio of **1a**/**2a**/**3a**	solvent	base	*T* (°C)	time (h)	**4a** yield (%)[b]	**4a'** yield (%)[b]
1	1:2:1	DCM	–	rt	24	22	13
2	1:2:1	CH_3CN	–	rt	24	11	18
3	1:2:1	DCE	–	rt	24	27	21
4	**1:2:1**	**THF**	–	**rt**	**24**	**52**	**12**
5	1:2:1	CH_3OH	–	rt	24	–	–
6	1:2:1	DCM	–	reflux	24	32	10
7	1:2:1	CH_3CN	–	reflux	24	24	15
9	1:2:1	DCE	–	reflux	24	28	12
10	1:2:1	THF	–	reflux	24	38	–
11	1:2:1	CH_3OH	–	reflux	24	–	–
12	1:2:1	THF	DABCO	rt	24	–	–
13	1:2:1	THF	DMAP	rt	24	–	–
14	1:1.5:1	THF	–	rt	24	42	10
15	1:2:1	THF	–	rt	12	35	trace
16	1:2:1	THF	–	rt	36	50	11
17	1:2:1	THF	–	0	24	35	trace

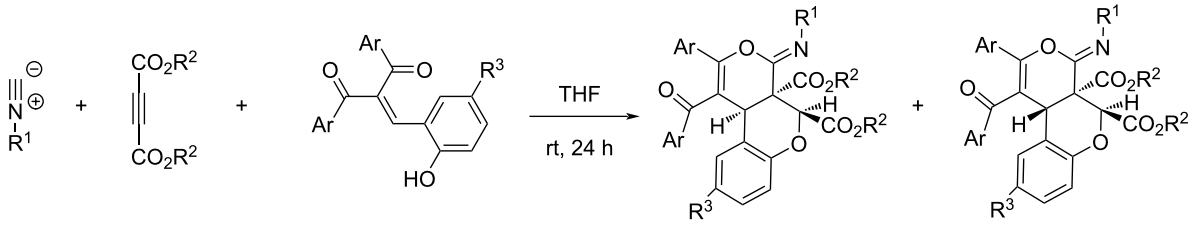
[a]Standard reaction conditions: cyclohexyl isocyanide (**1a**, 0.2 mmol), dimethyl but-2-ynedioate (**2a**), 2-(2-hydroxybenzylidene)-1,3-diphenylpropane-1,3-dione (**3a**, 0.2 mmol) and solvent (5.0 mL). [b]Isolated yields.

cyclo[2.2.2]octane) or DMAP (*N*,*N*-dimethylpyridin-4-amine) were introduced in the reaction (Table 1, entries 12 and 13). In addition, if less amount of dimethyl but-2-ynedioate (**2a**) was used, the yield of the product **4a** decreased to 42%, while the product **4a'** was obtained in 10% yield (Table 1, entry 14). Then, reaction time and temperature were also tested, which did not give good results (Table 1, entries 15–17). Therefore, the optimized reaction for the three-component reaction was successfully established at mild reaction conditions.

With the optimized reaction conditions in hands, the scope of the reaction was developed by employing various substrates. The results are summarized in Table 2. It can be found that the three-component reactions proceeded smoothly to give the desired major products **4a–n** and minor products **4a'–n'** in moderate yields, which can be successfully isolated by column chromatography. Both of cyclohexyl and *tert*-butyl isocyanides can be employed for the present transformation. The substituents on the aryl group showed little effect on the yields of the products. It should be pointed out that some minor products were not isolated due to too low yields.

The chemical structures of the compounds were fully characterized by various kinds of spectroscopies. For an example, the ^{1}H NMR spectrum of compound **4c** showed two singlets at 3.87 and 3.79 ppm for the two methyl groups of the ester and two singlets at 5.11, and 4.58 ppm for the two protons on the newly-formed chromene ring. On the other hand, the ^{1}H NMR spectrum of compound **4c'** showed two singlets at 3.77 and 3.69 ppm for the two methyl groups of the ester and two singlets at 5.46, and 3.85 ppm for the two protons on the newly-formed chromene ring. For determining the relative configuration of two diastereomers, the single crystal structures of the compounds **4c** (Figure 1) and **4c'** (Figure 2) were determined by X-ray diffraction. The corresponding single crystal data were listed in Table S1 (see Supporting Information File 1). From Figure 1, it can be seen that the two methoxycarbonyl groups are in *trans*-configuration to each other, while the proton atom and the methoxycarbonyl group on the two bridgehead carbon atoms in the chromene ring are in *cis*-position, which means that the pyranyl ring and the chromene ring was connected in *cis*-configuration. From Figure 2, it can be seen that the proton atom and the methoxycarbonyl group on the two bridgehead

Table 2: Synthesis of the pyrano[3,4-*c*]chromenes **4a–n** and **4a'–n'**.[a]



1 **2** **3** **4a–n** **4a'–n'**

entry	R^1	R^2	R^3	Ar	compd	yield (%)[b]	compd	yield (%)[b]
1	cyclohexyl	CH_3	H	Ph	**4a**	52	**4a'**	12
2	cyclohexyl	CH_3	OCH_3	Ph	**4b**	48	**4b'**	11
3	cyclohexyl	CH_3	Cl	Ph	**4c**	30	**4c'**	24
4	cyclohexyl	CH_3	Br	Ph	**4d**	33	**4d'**	24
5	cyclohexyl	C_2H_5	H	Ph	**4e**	33	**4e'**	–
6	cyclohexyl	C_2H_5	OCH_3	Ph	**4f**	31	**4f'**	–
7	cyclohexyl	C_2H_5	Cl	Ph	**4g**	28	**4g'**	–
8	cyclohexyl	C_2H_5	Br	Ph	**4h**	30	**4h'**	–
9	*t*-Bu	CH_3	H	Ph	**4i**	39	**4i'**	13
10	*t*-Bu	CH_3	OCH_3	Ph	**4j**	26	**4j'**	–
11	*t*-Bu	CH_3	Cl	Ph	**4k**	30	**4k'**	–
12	*t*-Bu	CH_3	Br	Ph	**4l**	32	**4l'**	10
13	cyclohexyl	CH_3	H	*p*-$CH_3OC_6H_5$	**4m**	30	**4m'**	–
14	*t*-Bu	CH_3	H	*p*-$CH_3OC_6H_5$	**4n**	28	**4n'**	–

[a]Standard reaction conditions: alkyl isocyanides **1** (0.2 mmol, 1.0 equiv), dialkyl but-2-ynedioates **2** (0.4 mmol, 2.0 equiv), 2-(2-hydroxybenzylidene)-1,3-diarylpropane-1,3-diones **3** (0.2 mmol, 1.0 equiv), THF (5.0 mL), rt, 24 h. [b]Isolated yields.

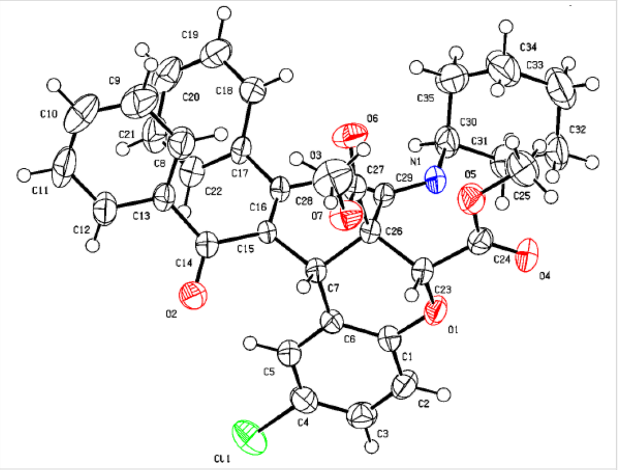


Figure 1: Single crystal structure of compound **4c** (ORTEP-drawing, thermal ellipsoids set at the 30% probability level).

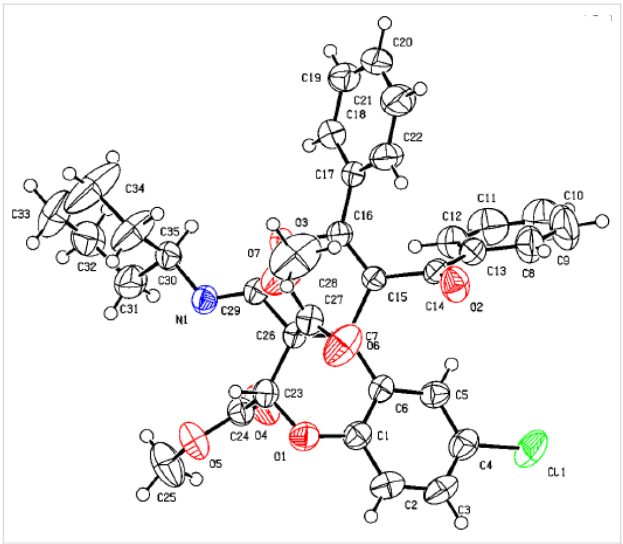
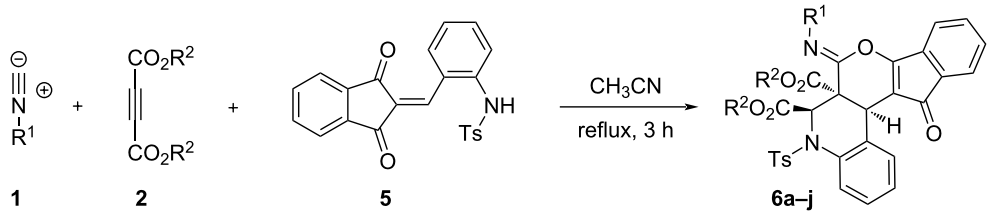


Figure 2: Single crystal structure of compound **4c'** (ORTEP-drawing, thermal ellipsoids set at the 30% probability level).

carbon atoms are in *trans*-position, which means that the pyranyl ring and the chromene ring was connected together in *trans*-configuration. The two methoxycarbonyl groups still exist on the *trans*-configuration. Therefore, the two diastereomers of pyrano[3,4-*c*]chromenes **4a–n** and **4a'–n'** resulted from the *cis*-/*trans*-configuration of the fused pyranyl and chromene rings.

For developing the scope of this three-component reaction, 2-(2-*N*-tosylaminobenzylidene)-1,3-indanedione (**5**) were also employed in the reaction. The three-component reaction of cyclohexyl isocyanide (**1a**), dimethyl but-2-ynedioate (**2a**) and 2-(2-*N*-tosylaminoxbenzylidene)-1,3-indanedione (**5**) in tetrahydrofuran at room temperature proceeded very sluggish. Further examination of the reaction conditions showed that the three-component reaction in refluxing acetonitrile for three hours gave the expected functionalized tetrahydroindeno[2',1':5,6]pyrano[3,4-*c*]quinoline **6a** in 60% yield (Table 3, entry 1). The similar reactions with other

Table 3: Synthesis of the tetrahydroindeno[2',1':5,6]pyrano[3,4-*c*]quinolines **6a–j**.[a]



1 **2** **5** **6a–j**

entry	R^1	R^2	compd	yield (%)[b]
1	cyclohexyl	CH_3	**6a**	60
2	*t*-Bu	CH_3	**6b**	54
3	Bn	CH_3	**6c**	40
4	*p*-$CH_3OC_6H_4$	CH_3	**6d**	45
5	*p*-BrC_6H_4	CH_3	**6e**	38
6	cyclohexyl	C_2H_5	**6f**	47
7	*t*-Bu	C_2H_5	**6g**	40
8	Bn	C_2H_5	**6h**	23
9	*p*-$CH_3OC_6H_4$	C_2H_5	**6i**	37
10	*p*-BrC_6H_4	C_2H_5	**6j**	28

[a]Reaction conditions: alkyl isocyanide **1** (0.2 mmol, 1.0 equiv), dialkyl but-2-ynedioate **2** (0.5 mmol, 2.5 equiv), 2-(2-*N*-tosylaminobenzylidene)-1,3-indanedione (**5**, 0.2 mmol, 1.0 equiv), CH_3CN (5.0 mL), reflux, 3 h. [b]Isolated yields.

isocyanides such as *tert*-butyl, benzyl, *p*-methoxyphenyl and *p*-bromophenyl isocyanides also afforded tetrahydroindeno[2',1':5,6]pyrano[3,4-*c*]quinolines **6b–e** in 38–54% yields (Table 3, entries 2–5). When diethyl but-2-ynedioate was used in the reaction, the three-component reaction resulted in the tetrahydroindeno[2',1':5,6]pyrano[3,4-*c*]quinolines **6f–j** in lower yields (Table 3, entries 6–10). The TLC analysis and ^{1}H NMR spectra of the crude products clearly indicated that only one diastereomer was predominately produced in the reaction, while other diastereomers were not detected in the reaction. This result is different to the above mentioned three-component reaction for the formation of two diastereomers **4** and **4'**, which might be due to restriction of the polycyclic rings including the indanone skeleton. The single crystal structures of compounds **6a** and **6b** were also determined (Figure 3 and Figure 4). The single crystal data were listed in Table S2 (see Supporting Information File 1). From Figure 3 and Figure 4 it can be seen that the newly-formed pyrene ring and tetrahydroquinoline ring were fused in *cis*-form. The proton and the methoxycarbonyl group are in *cis*-position. The two methoxycarbonyl groups exist on *trans*-configuration. Therefore, the compounds **6a–j** have the same relative configuration to that of the major products **4a–n**, which also indicated that the two three-component reactions have a similar reaction mechanism and steric controlling factors.

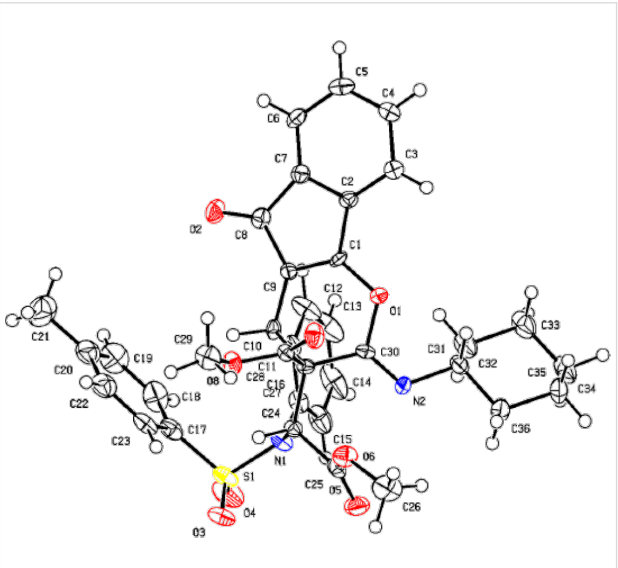


Figure 3: Single crystal structure of compound **6a** (ORTEP-drawing, thermal ellipsoids set at the 30% probability level).

In order to explain the formation of above functionalized fused chromenes, a plausible reaction mechanism is proposed on the basis of the previously reported works [46-53] and the present obtained experimental results (Scheme 2). At first, the nucleophilic addition of alkyl isocyanide **1** to alkyl but-2-ynedioate **2** gave the well-known 1,4-dipolar intermediate **A**. Secondly, a proton exchange between 1,4-dipolar intermediate **A** to 2-(2-hydroxybenzylidene)-1,3-diarylpropane-1,3-dione **3** resulted in the intermediate **B** and a phenoxide ion **C**. Thirdly, the nucleophilic addition of the phenoxide **C** to the intermediate **B** afforded adduct **D**. Sequentially, an intramolecular Michael addition of the carbanion to C=C bond in the adduct **D** produced the intermediate **E** with a chromane skeleton. Finally, the nueleophilic addition of the enolate ion to the nitrilium ion in the intermediate **E** gave the diatereomeric pyrano[3,4-*c*]chromenes **4** and **4'**. Because each reaction step is equilibrium reaction in the cyclization process, the reaction selectively gave the more stable compounds **4a–n** (*cis*-fused ring) as major products and less stable compounds **4a'–n'** (*trans*-fused ring) as minor products. On the other hand, formation of product **6** also followed this reaction mechanism. A proton exchange between the 1,4-dipolar intermediate **A** to 2-(2-*N*-tosylaminobenzylidene)-1,3-indanedione **5** produced the intermediate **B** and an amino anion **F**. Then, the nucleophilic addition of the amino anion **F** to the intermediate **B** afforded the adduct **G**, which was converted to the intermediate **H** by an intramolecular Michael addition of the carbanion to the C=C bond. Finally, the coupling of the nitrilium ion and the enolate in intermediate **H** gave the functionalized tetrahydroindeno[2',1':5,6]pyrano[3,4-*c*]quinolines **6**. It might be due to the rigid ring of the indanone, only one diastereomer (*cis*-fused ring) was formed in the reaction.

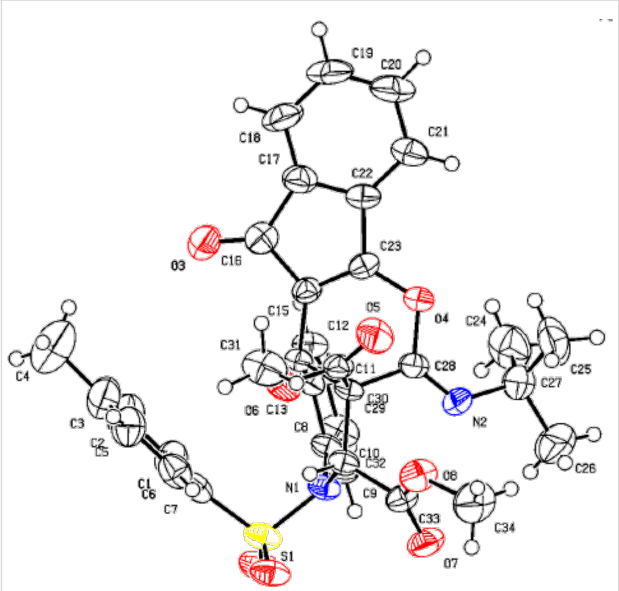
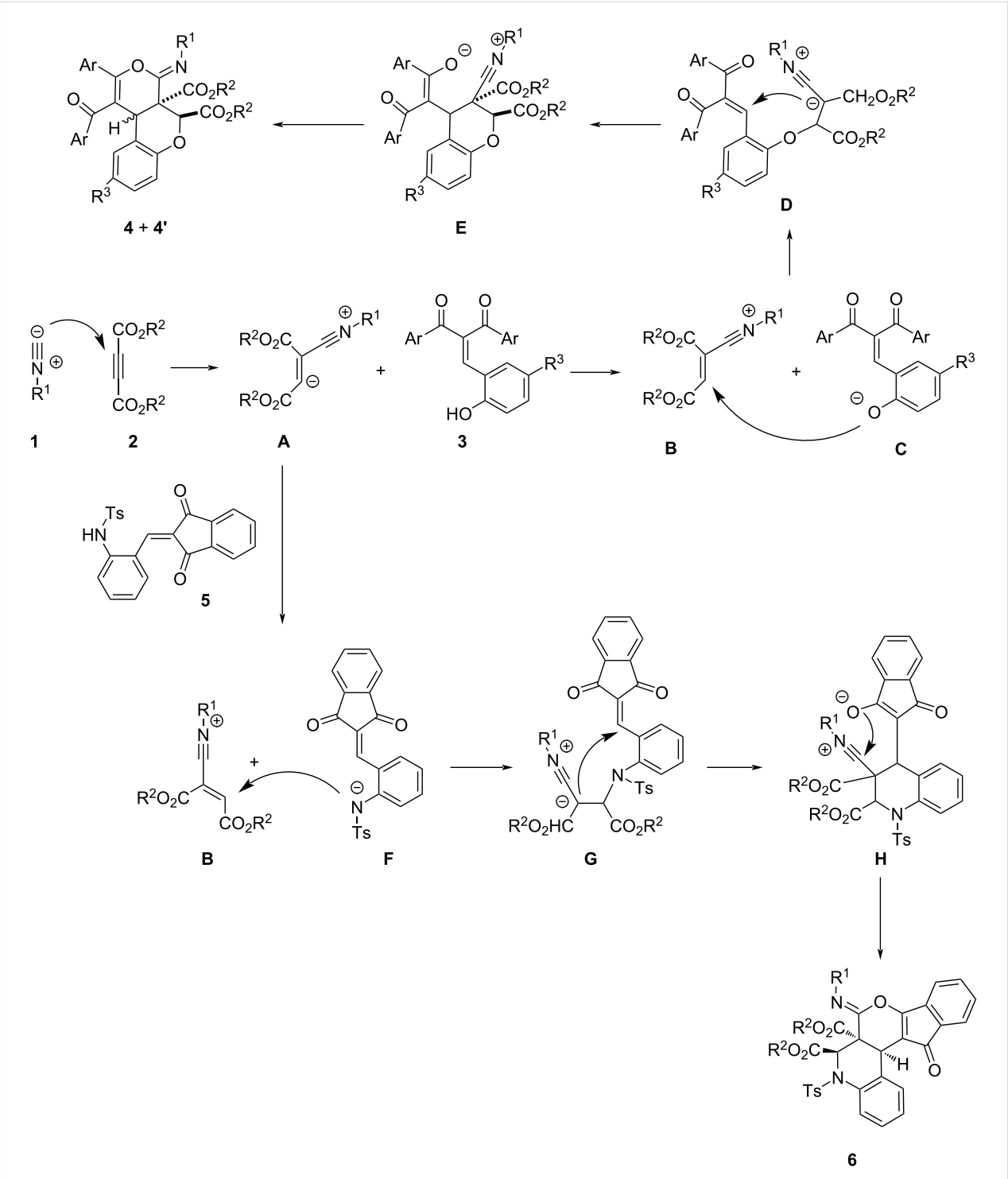


Figure 4: Single crystal structure of compound **6b** (ORTEP-drawing, thermal ellipsoids set at the 30% probability level).

For demonstrating the synthetic value of this three-component reaction, arylamines were employed to replacing alkyl cyanides



Scheme 2: Proposed reaction mechanism for the syntheses of compounds **4** and **6**.

in the three-component reaction. However, the three-component reaction of arylamines **7**, dialkyl but-2-ynedioates **2** and 2-(2-hydroxybenzylidene)-1,3-diphenylpropane-1,3-dione **3** in tetrahydrofuran did not give the expected polycyclic products. TLC monitoring indicated that the nucleophilic addition of arylamine to dimethyl but-2-ynedioate gave the well-known dimethyl 2-(arylamino)maleate as the isolated product [61-65], while 2-(2-hydroxybenzylidene)-1,3-diphenylpropane-1,3-dione **3** did not take part in the further reaction. Then, a one-pot two-step reaction procedure was employed. The reaction of

arylamines **7** and dialkyl but-2-ynedioates **2** in dichloromethane at room temperature for half an hour resulted in the expected known dimethyl 2-(arylamino)maleate. Then, 2-(2-hydroxybenzylidene)-1,3-diphenylpropane-1,3-dione **3** and Lewis acid catalyst boron trifluoride etherate were introduced in the reaction mixture. The further reaction was carried out in refluxing dichloromethane for six hours. The poly-substituted chromenes **8a–p** were obtained in 40–65% yields (Table 4). Various substituted arylamines can be successfully employed in the reaction. However, benzylamine and *n*-butylamine cannot be used in the reaction, which gave very complicated mixtures of products. The chemical structures of the substituted chromenes **8a–p** were fully characterized by IR, ^{1}H and ^{13}C NMR spectroscopy as well as HRMS spectrometry. The single crystal structure of the compound **8j** was determined (Figure 5). It can be seen that the phenylamino group and the moiety of dimethyl fumarate did not participate in the cyclization process and only acted as a substituent on the chromene ring. The two methoxycarbonyl groups on the C=C bond are in *trans*-configuration. The chromene ring results from the annulation of the 1,3-diphenylpropane-1,3-dione unit. All attempts of further cyclization of the arylamino group with the carbonyl

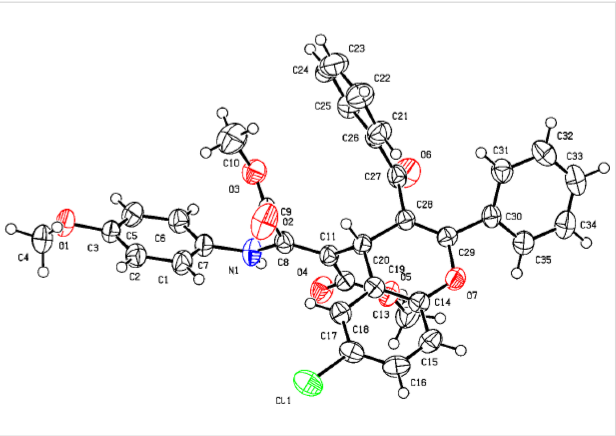
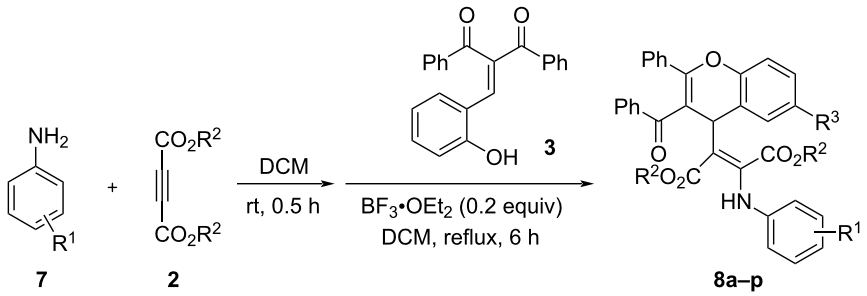


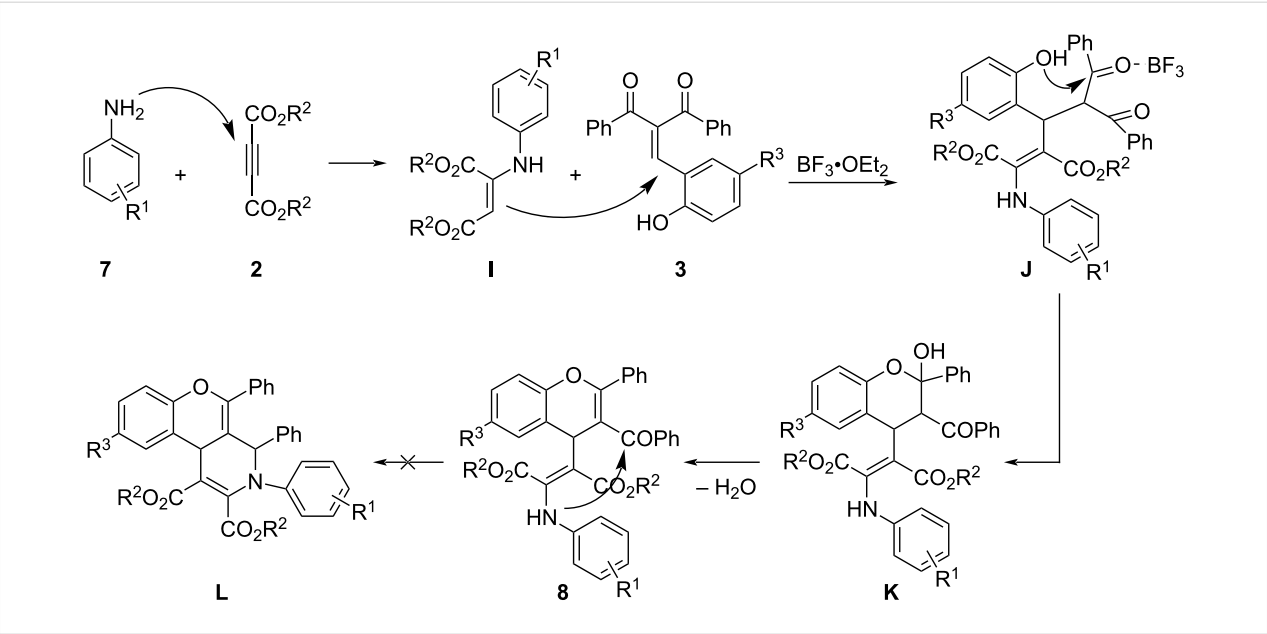
Figure 5: Single crystal structure of compound **8j** (ORTEP-drawing, thermal ellipsoids set at the 30% probability level).

Table 4: Synthesis of the functionalized chromenes **8a–p**.[a]



entry	R^1	R^2	R^3	compd	yield (%)[b]
1	*m*-CH_3	CH_3	OCH_3	**8a**	62
2	*m*-CH_3	CH_3	H	**8b**	57
3	*m*-CH_3	CH_3	Cl	**8c**	45
4	*m*-CH_3	CH_3	Br	**8d**	40
5	*m*-Cl	CH_3	OCH_3	**8e**	65
6	*m*-Cl	CH_3	H	**8f**	60
7	*m*-Cl	CH_3	Cl	**8g**	41
8	*p*-CH_3O	CH_3	OCH_3	**8h**	53
9	*p*-CH_3O	CH_3	H	**8i**	45
10	*p*-CH_3O	CH_3	Cl	**8j**	40
11	H	CH_3	OCH_3	**8k**	64
12	H	CH_3	H	**8l**	60
13	H	CH_3	Cl	**8m**	52
14	*m*-CH_3	C_2H_5	OCH_3	**8n**	49
15	*m*-CH_3	C_2H_5	H	**8o**	45
16	*m*-CH_3	C_2H_5	Cl	**8p**	40

[a]Standard reaction conditions: arylamine **7** (0.2 mmol, 1.0 equiv), dialkyl but-2-ynedioate **2** (0.4 mmol, 2.0 equiv), DCM (5 mL), rt, 0.5 h, 2-(2-hydroxybenzylidene)-1,3-diphenylpropane-1,3-dione **3** (0.2 mmol, 1.0 equiv), $BF_3{\cdot}OEt_2$ (0.4 mmol, 0.2 equiv), 40 °C, 6 h. [b]Isolated yields.



Scheme 3: Proposed reaction mechanism for the formation of chromenes **8**.

group in the obtained compounds **8** to form a pyridyl ring were not successful. These results clearly show that alkyl isocyanides have very different reactivity to that of arylamines.

A plausible reaction mechanism was also proposed for the formation of chromenes **8** (Scheme 3) [61-65]. Firstly, a nucleophilic addition of arylamine **7** to dialkyl but-2-ynedioate **2** gave the well-known dialkyl 2-(arylamino)maleate **I**. Secondly, the addition of the enamino unit of intermediate **I** to the C=C bond in reagent **3** gave adduct intermediate **J**. In the presence of Lewis acid, the intramolecular addition of the hydroxy group to the carbonyl group in the intermediate **J** afforded the intermediate **K**, which was converted to the isolated product **8** by a further dehydration process. The further annulation to give the expected chromeno[3,4-*c*]pyridine **L** by the addition of an arylamino group to another carbonyl group did not happen in the reaction.

Conclusion

In summary, we have investigated three-component reactions of alkyl isocyanides, dialkyl but-2-ynedioates and various unsaturated diketones. These reactions successfully provided convenient synthetic methods for the formation of functionalized pyrano[3,4-*c*]chromenes and tetrahydroindeno[2',1':5,6]pyrano[3,4-*c*]quinolines in moderate to good yields. By using arylamines instead of alkyl isocyanides in the three-component reaction, functionalized chromenes with 2-(arylamino)maleate as substituent were also prepared in moderate to good yields. The relative configuration of the polycyclic compounds was clearly determined and a plausible formation mechanism for these polycyclic compounds were proposed. The advantages of this reaction included the use of readily available materials, a broad substrate scope, mild reaction conditions, high molecular diversity and high atomic economy. The potential applications of these multicomponent reactions might be significant in organic and medicinal chemistry.

Supporting Information

The crystallographic data of compounds **4c** (CCDC 2556317), **4c'** (CCDC 2556316), **6a** (CCDC 2556318), **6b** (CCDC 2556319), **8j** (CCDC 2556320) have been deposited at the Cambridge Crystallographic Database Centre (http://www.ccdc.cam.ac.uk).

Supporting Information File 1

Experiment procedures, ^{1}H and ^{13}C NMR as well as HRMS spectra of the synthesized compounds.
[https://www.beilstein-journals.org/bjoc/content/supplementary/1860-5397-22-135-S1.pdf]

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Conflict of Interest

The authors declare that they do not have any conflicts of interest.

Author Contributions

Xinyu Zhang: data curation; investigation. Dong-Mei Liu: investigation; software. Jing Sun: formal analysis. Chao-Guo Yan: project administration; writing – review & editing. Ying Han: supervision.

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Data Availability Statement

All data that supports the findings of this study is available in the published article and/or the supporting information of this article.

References

1. Zhu, J. *Eur. J. Org. Chem.* **2003,** 1133–1144. doi:10.1002/ejoc.200390167
2. Lygin, A. V.; de Meijere, A. *Angew. Chem., Int. Ed.* **2010,** *49,* 9094–9124. doi:10.1002/anie.201000723
3. Giustiniano, M.; Basso, A.; Mercalli, V.; Massarotti, A.; Novellino, E.; Tron, G. C.; Zhu, J. *Chem. Soc. Rev.* **2017,** *46,* 1295–1357. doi:10.1039/c6cs00444j
4. Gulevich, A. V.; Zhdanko, A. G.; Orru, R. V. A.; Nenajdenko, V. G. *Chem. Rev.* **2010,** *110,* 5235–5331. doi:10.1021/cr900411f
5. Dömling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000,** *39,* 3168–3210. doi:10.1002/1521-3773(20000915)39:18<3168::aid-anie3168>3.0.co;2-u
6. Nair, V.; Rajesh, C.; Vinod, A. U.; Bindu, S.; Sreekanth, A. R.; Mathen, J. S.; Balagopal, L. *Acc. Chem. Res.* **2003,** *36,* 899–907. doi:10.1021/ar020258p
7. Qiu, G.; Ding, Q.; Wu, J. *Chem. Soc. Rev.* **2013,** *42,* 5257–5269. doi:10.1039/c3cs35507a
8. Estévez, V.; Villacampa, M.; Menéndez, J. C. *Chem. Soc. Rev.* **2014,** *43,* 4633–4657. doi:10.1039/c3cs60015g
9. Lenarduzzi D'Emilio, N. A.; Paz Armero, P. K.; Mendoza Salgado, A. R.; Simonetti, S. O.; Bracca, A. B. J.; Larghi, E. L.; Kaufman, T. S. *Org. Biomol. Chem.* **2026,** *24,* 1965–1996. doi:10.1039/d5ob02009c
10. Shan, Y.; Lv, D.; Zhang, X.; Wang, J.; Chen, D. *Chem. Commun.* **2026,** *62,* 1391–1408. doi:10.1039/d5cc05745k
11. Kochnev, I. A.; Barkov, A. Y. *New J. Chem.* **2025,** *49,* 20254–20263. doi:10.1039/d5nj03333k
12. Kumar, A.; Mishra, P. K.; Verma, A. K. *Chem. Commun.* **2023,** *59,* 7263–7266. doi:10.1039/d3cc01586f
13. Wan, J.-P.; Liu, Y. *RSC Adv.* **2012,** *2,* 9763–9777. doi:10.1039/c2ra21406g
14. Sadjadi, S.; Heravi, M. M.; Nazari, N. *RSC Adv.* **2016,** *6,* 53203–53272. doi:10.1039/c6ra02143c
15. Ma, X.; Gao, Z.; Niu, J.; Shao, W.; Yan, S.; Zhang, S.; Zhang, W. *Beilstein J. Org. Chem.* **2025,** *21,* 2202–2210. doi:10.3762/bjoc.21.167
16. Zhou, W.; Lu, S.; Zhao, X.; Wang, H.; Ding, C.-H.; Gao, M.; Xu, B. *Org. Lett.* **2026,** *28,* 5447–5452. doi:10.1021/acs.orglett.6c01047
17. Zhang, T.; Wang, W.; Chen, M.; Hu, J.; Liu, P.; Sun, P. *Org. Lett.* **2026,** *28,* 3191–3195. doi:10.1021/acs.orglett.6c00189
18. Fardi, E.; Rafiee, F. *Tetrahedron* **2026,** *198,* 135346. doi:10.1016/j.tet.2026.135346
19. Yu, S.; Xu, J.; Li, X.; Yang, X.-Y.; Lei, J.; Lv, M.-L.; Chen, Z.-Z. *J. Org. Chem.* **2026,** *91,* 5280–5292. doi:10.1021/acs.joc.5c02998
20. Li, Y.-G.; Wang, C.-C.; Ma, Z.-W.; Chen, X.-P.; Zhu, X.; Hao, X.-Q. *Tetrahedron* **2025,** *188,* 134985. doi:10.1016/j.tet.2025.134985
21. He, Y.; Shen, X.-Y.; Ding, Y.; Wang, Y.-C.; Xie, Y.-Y.; Pan, Y.-M. *Green Chem.* **2026,** *28,* 4795–4831. doi:10.1039/d6gc00161k
22. Mi, Y.-H.; Wang, Z.-Y.; Wang, Y.-H.; Wang, K.; Zhang, Y.; Yang, Y.-Q.; Huang, X.-Y.; Zhang, S.-X.; Zhao, H.-W. *Eur. J. Org. Chem.* **2026,** *29,* e202501126. doi:10.1002/ejoc.202501126
23. Chen, L.; Xiong, D.; Yang, Z.; Chen, Y.; Xiao, J.; Tian, Y.; Zheng, J. *Org. Chem. Front.* **2024,** *11,* 5868–5875. doi:10.1039/d4qo01369g
24. Dömling, A. *J. Org. Chem.* **2023,** *88,* 5242–5247. doi:10.1021/acs.joc.2c00792
25. Massarotti, A.; Brunelli, F.; Aprile, S.; Giustiniano, M.; Tron, G. C. *Chem. Rev.* **2021,** *121,* 10742–10788. doi:10.1021/acs.chemrev.1c00143
26. Kalhans, P.; Singh, A.; Mishra, S.; Pandey, S. *Org. Biomol. Chem.* **2025,** *23,* 3243–3269. doi:10.1039/d4ob02094d
27. Nazeri, M. T.; Nasiriani, T.; Norouzi, M.; Torabi, S.; Vakili, M. A.; Shaabani, A. *Org. Chem. Front.* **2026,** *13,* 6316–6411. doi:10.1039/d6qo00608f
28. Flores-Reyes, J. C.; Islas-Jácome, A.; González-Zamora, E. *Org. Chem. Front.* **2021,** *8,* 5460–5515. doi:10.1039/d1qo00313e
29. Ojeda-Carralero, G. M.; Ceballos, L. G.; Coro, J.; Rivera, D. G. *ACS Comb. Sci.* **2020,** *22,* 475–494. doi:10.1021/acscombsci.0c00111
30. Nazeri, M. T.; Farhid, H.; Mohammadian, R.; Shaabani, A. *ACS Comb. Sci.* **2020,** *22,* 361–400. doi:10.1021/acscombsci.0c00046
31. Mathiyazhagan, A. D.; Anilkumar, G. *Org. Biomol. Chem.* **2019,** *17,* 6735–6747. doi:10.1039/c9ob00847k
32. Nazeri, M. T.; Ghasemi, M.; Ahmadi, M.; Shaabani, A.; Notash, B. *J. Org. Chem.* **2023,** *88,* 13504–13519. doi:10.1021/acs.joc.3c01013
33. Li, Y.; Kopcha, W. P.; Emge, T. J.; Sun, Y.; Zhang, J. *Org. Lett.* **2021,** *23,* 8867–8872. doi:10.1021/acs.orglett.1c03371
34. Bankura, A.; Saha, J.; Maity, R.; Das, I. *Adv. Synth. Catal.* **2021,** *363,* 1014–1021. doi:10.1002/adsc.202001376
35. Farhid, H.; Araghi, H. M.; Shaabani, A.; Notash, B. *J. Mol. Struct.* **2023,** *1292,* 136143. doi:10.1016/j.molstruc.2023.136143
36. Ansari, M. D.; Sagir, H.; Yadav, V. B.; Yadav, N.; Verma, A.; Shakya, S.; Singh, M.; Siddiqui, I. R. *Mol. Diversity* **2023,** *27,* 1853–1866. doi:10.1007/s11030-022-10532-3
37. Vahedi, M. M.; Asghari, S.; Tajbakhsh, M.; Mohseni, M.; Khalilpour, A. *J. Mol. Struct.* **2023,** *1284,* 135446. doi:10.1016/j.molstruc.2023.135446
38. Nazeri, M. T.; Ahmadi, M.; Ghasemi, M.; Shaabani, A.; Notash, B. *Org. Biomol. Chem.* **2023,** *21,* 4095–4108. doi:10.1039/d3ob00250k
39. Hasan, M.; Peshkov, A. A.; Shah, S. A. A.; Belyaev, A.; Lim, C.-K.; Wang, S.; Peshkov, V. A. *Beilstein J. Org. Chem.* **2025,** *21,* 915–925. doi:10.3762/bjoc.21.74
40. Yavari, I.; Ravaghi, P.; Safaei, M. *Synthesis* **2022,** *54,* 1870–1876. doi:10.1055/s-0041-1737817
41. Nair, V.; Vinod, A. U.; Rajesh, C. *J. Org. Chem.* **2001,** *66,* 4427–4429. doi:10.1021/jo001714v
42. Rahmani, F.; Darehkordi, A. *Synlett* **2017,** *28,* 1224–1226. doi:10.1055/s-0036-1588732
43. Nair, V.; Vinod, A. U.; Abhilash, N.; Menon, R. S.; Santhi, V.; Varma, R. L.; Viji, S.; Mathew, S.; Srinivas, R. *Tetrahedron* **2003,** *59,* 10279–10286. doi:10.1016/j.tet.2003.10.052
44. Wang, C.-C.; Ma, Z.-W.; Qu, Y.-L.; Liu, Z.-J.; Chen, X.-P.; Zhou, J.; Chen, Y.-J. *Chem. – Asian J.* **2020,** *15,* 560–563. doi:10.1002/asia.201901780
45. Nazeri, M. T.; Shaabani, A.; Notash, B. *Org. Biomol. Chem.* **2021,** *19,* 3722–3734. doi:10.1039/d0ob02339f

46. Ma, W.; Han, Y.; Sun, J.; Yan, C. *Chin. J. Org. Chem.* **2021,** *41,* 3180–3191. doi:10.6023/cjoc202103034
47. He, Y.-W.; Ma, W.-Q.; Han, Y.; Sun, J.; Yan, C.-G. *J. Org. Chem.* **2023,** *88,* 14911–14927. doi:10.1021/acs.joc.3c01246
48. Huang, L.; Han, Y.; Sun, J.; Sun, Q.; Yan, C.-G. *Org. Biomol. Chem.* **2023,** *21,* 6028–6033. doi:10.1039/d3ob00769c
49. He, Y.-W.; Huang, L.; Huang, K.; Yan, C.-G.; Sun, J.; Han, Y. *J. Org. Chem.* **2024,** *89,* 10854–10866. doi:10.1021/acs.joc.4c01142
50. Chen, X.-Y.; Han, Y.; Sun, J.; Yan, C.-G. *Beilstein J. Org. Chem.* **2024,** *20,* 1436–1443. doi:10.3762/bjoc.20.126
51. Huang, L.; Ma, W.-Q.; Sun, J.; Han, Y.; Yan, C.-G. *Org. Biomol. Chem.* **2025,** *23,* 3224–3230. doi:10.1039/d5ob00206k
52. Zhang, X.; Huang, L.; Sun, J.; Han, Y.; Yan, C.-G. *Eur. J. Org. Chem.* **2026,** *29,* e202501219. doi:10.1002/ejoc.202501219
53. Zhan, S.-C.; Huang, L.; Sun, J.; Yan, C.-G. *Tetrahedron* **2025,** *185,* 134853. doi:10.1016/j.tet.2025.134853
54. Tang, T.; Han, Y.; Yan, C.-G.; Huang, K.; Sun, J. *Eur. J. Org. Chem.* **2024,** *27,* e202400777. doi:10.1002/ejoc.202400777
55. Liu, X.; Wang, D.; Sun, J.; Yan, C.-G. *J. Mol. Struct.* **2024,** *1304,* 137684. doi:10.1016/j.molstruc.2024.137684
56. Xiao, Z.-Y.; Sun, J.; Yan, C.-G. *Beilstein J. Org. Chem.* **2025,** *21,* 286–295. doi:10.3762/bjoc.21.21
57. Zhang, X.; Xu, F.; Kou, Z.; Sun, J.; Yan, C.-G.; Han, Y. *J. Mol. Struct.* **2025,** *1345,* 143025. doi:10.1016/j.molstruc.2025.143025
58. Tang, T.; Zhan, S.-C.; Sun, J.; Han, Y.; Yan, C.-G. *J. Mol. Struct.* **2025,** *1347,* 143070. doi:10.1016/j.molstruc.2025.143070
59. Chen, X.; Sun, J.; Han, Y.; Yan, C.-G. *J. Org. Chem.* **2025,** *90,* 2889–2906. doi:10.1021/acs.joc.4c02525
60. Liu, D.-M.; Chen, X.; Sun, J.; Yan, C.-G. *J. Mol. Struct.* **2026,** *1357,* 145292. doi:10.1016/j.molstruc.2026.145292
61. Nair, V.; Menon, R. S.; Sreekanth, A. R.; Abhilash, N.; Biju, A. T. *Acc. Chem. Res.* **2006,** *39,* 520–530. doi:10.1021/ar0502026
62. Shaabani, A.; Maleki, A.; Rezayan, A. H.; Sarvary, A. *Mol. Diversity* **2011,** *15,* 41–68. doi:10.1007/s11030-010-9258-1
63. Han, Y.; Sun, J.; Sun, Y.; Gao, H.; Yan, C. *Chin. J. Org. Chem.* **2012,** *32,* 1577–1586. doi:10.6023/cjoc201206008
64. Li, X.; Wang, J.-Y.; Yu, W.; Wu, L.-M. *Tetrahedron* **2009,** *65,* 1140–1146. doi:10.1016/j.tet.2008.11.095
65. Jiang, H.-F.; Li, J.-H.; Chen, Z.-W. *Tetrahedron* **2010,** *66,* 9721–9728. doi:10.1016/j.tet.2010.10.041

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